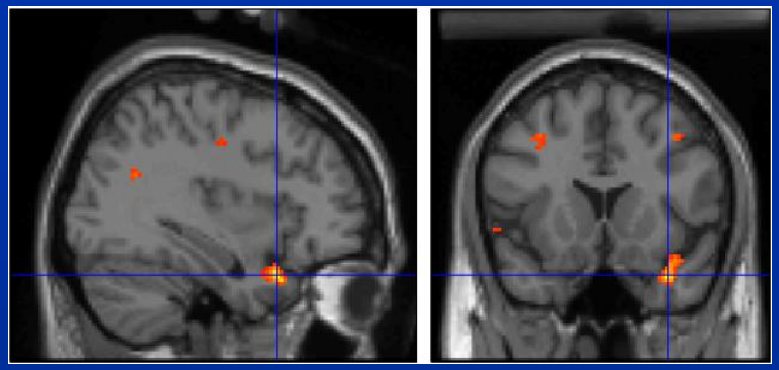

What Brain Centers Are Linked to Tinnitus- Related Distress? –An f-MRI Study

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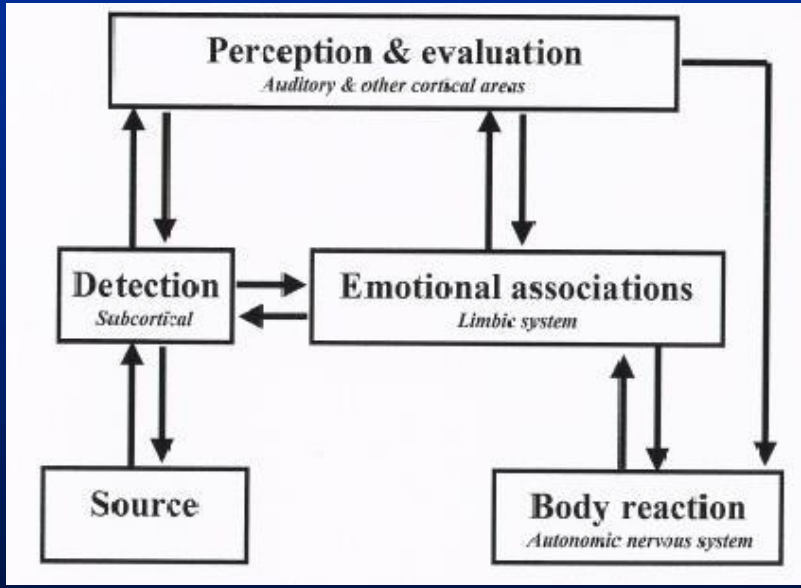
Aim and Approach

Aim of the study:

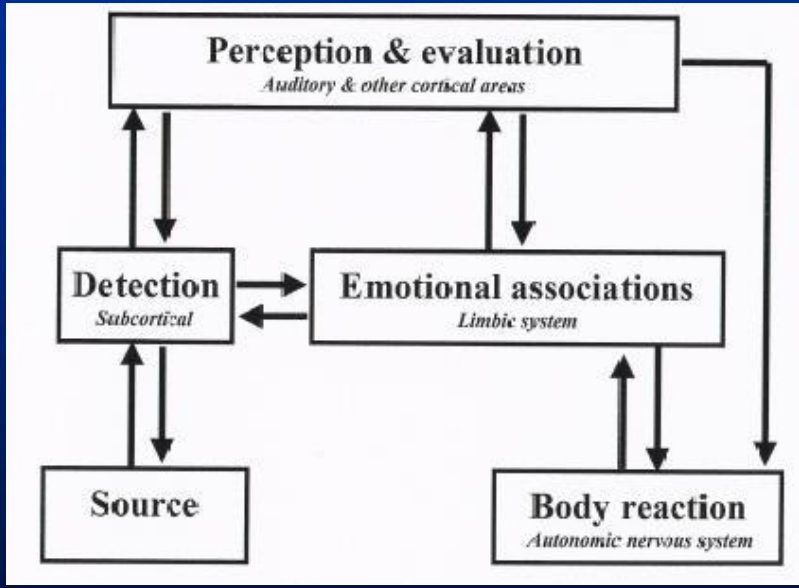
- **To delineate brain areas associated with tinnitus related distress.**

- **Approach**
  - **The Neurophysiological Model of Tinnitus:**
    - **Perception of Tinnitus**
    - **(Negative) Emotional reactions to the tinnitus signal.**
  - **Reactions to tinnitus are specific to the pattern of sound the patient perceives.**



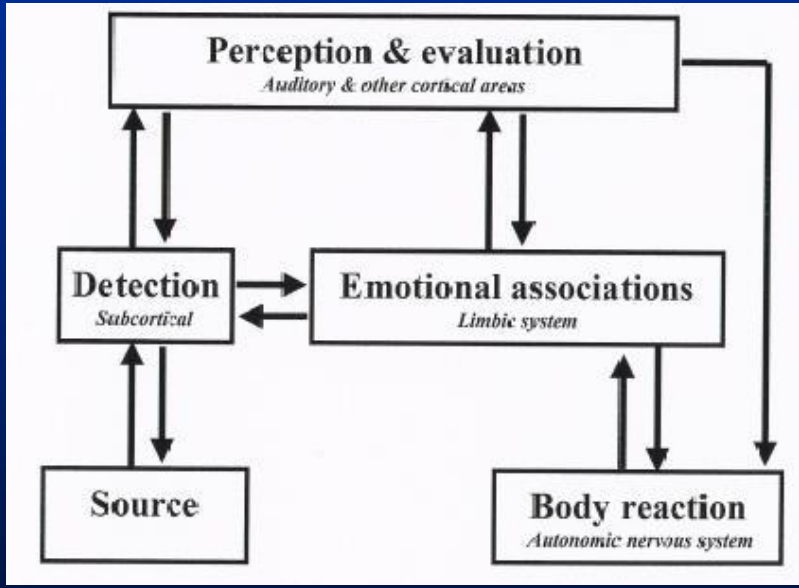
Aim and Approach

- Approach
  - Stimulating tinnitus patients using a reconstructed tinnitus sound should activate the network involved in the tinnitus-evoked emotional processing
  - Activation by the reconstructed tinnitus sound, but with spectrum shifted in frequency, should evoke a smaller reaction or should be ineffective.



Aim and Approach

- Approach
  - Looking at the difference between the BOLD responses evoked by the shifted tone and the reconstructed tinnitus, activity specific to the tinnitus perceived by the patient should result and should show some correlation with tinnitus-related distress

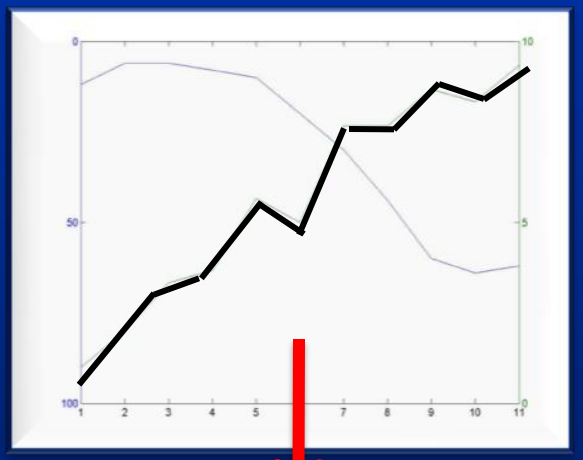


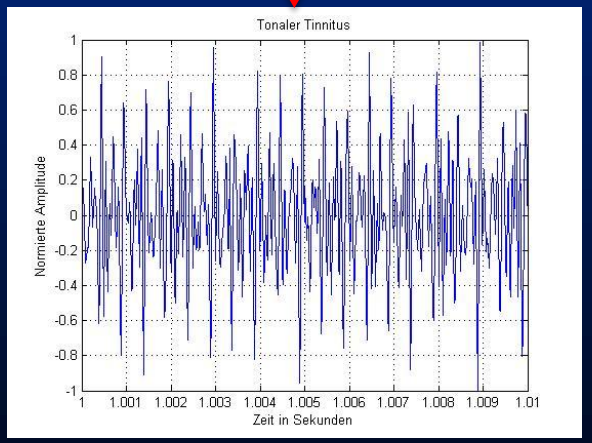
Subjects

- 61 subjects (35 tinnitus patients, 26 control subjects without tinnitus).
- Gender
  - Tinnitus subjects: 26♂, 9♀
  - Control subjects: 13♂, 13♀
- Age
  - Tinnitus subjects: 22-68 y (mean 49,3 y)
  - Control subjects: 24-64 y (mean 46,3 y)
- Tinnitus severity: low (grade 1 and 2 according to Goebel and Hiller score) in 29 patients, high (grade 3 and 4) in 6 patients.

Tinnitus Reconstruction Based on psychoacoustic Tinnitus Spectrum

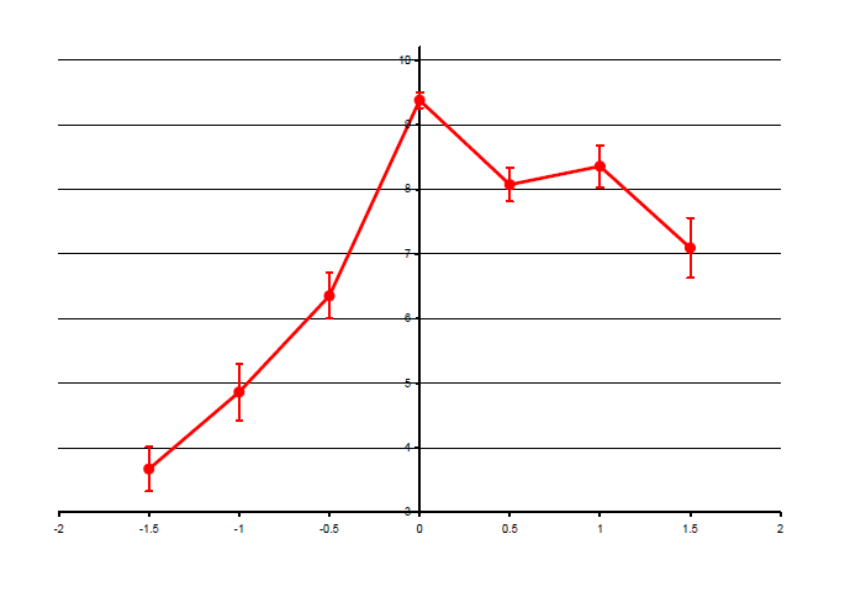
- Presentation of standard audiometric tones at the level of tinnitus loudness in randomized order (3 times).
- Judgement to what degree the tone presented contributes to the perceived tinnitus of the patient (VAS 0 to 10).
- Tinnitus reconstruction based on these responses using specific algorithms, and then fine tuned by interaction with a patient.





Tinnitus Reconstruction Based on psychoacoustic Tinnitus Spectrum

- All patients judged the similarity of the reconstructed tinnitus with the perceived tinnitus sound to be at least 8 on VAS 0 to 10.
- The activation evoked by the reconstructed tinnitus sound has been compared to activation evoked by this sound but with specturm shifted by 1,5 octaves.
- Non tinnitus patients were stimulated using a reconstructed tinnitus sound of a tinnitus patients showing high tinnitus related distress.



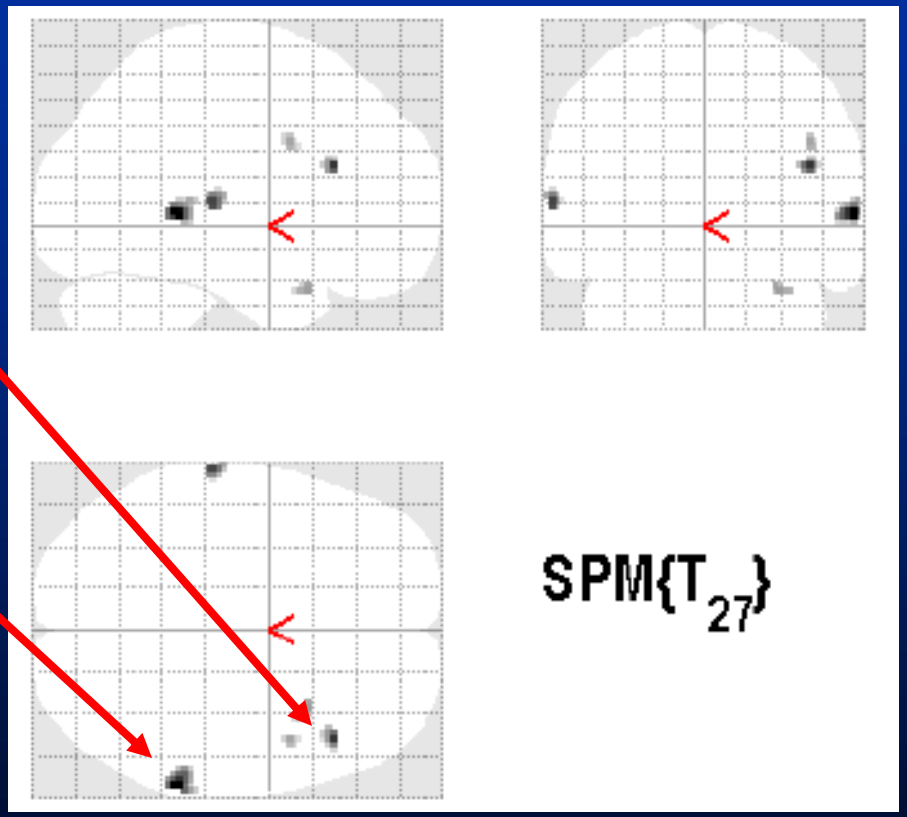
Functional MRI

- **1.5 Tesla MRI scanner with a standard head coil (Siemens Sonata, Erlangen Germany)**
- **36 slices of T2* weighted transverse echo-planar images (TR 5.04 s, TA 2.965 ms, TE 50 ms) with BOLD contrasts for functional analysis**
- **Structural MRI data were acquired using a T1-weighted, sagittally planned MPRAGE (magnetizationprepared rapid-acquired gradient echoes) sequence with a spatial resolution of 1mm×1mm×1mm isotrop (TR: 1900 ms,TE3.93 ms, TI 1100 ms, FA15◦).**

Results (I)

Contrast Tinnitus Tone Stimulation versus Silence (Tinnitus Subjects)

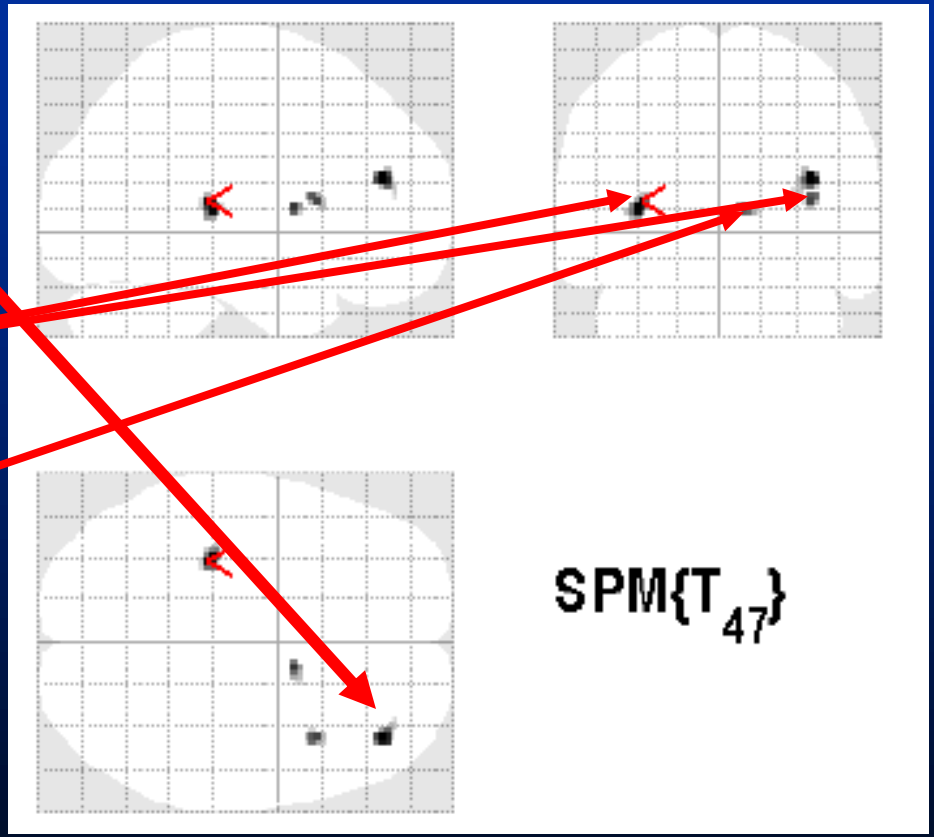
- Right Superior temporal gyrus
- Middle and inferior frontal gyrus (Brodman areas 46, 47 and 9)



Results (II)

Contrast Tinnitus Tone Stimulation versus Silence (Tinnitus-Subjects compared to Non-Tinnitus-Subjects)

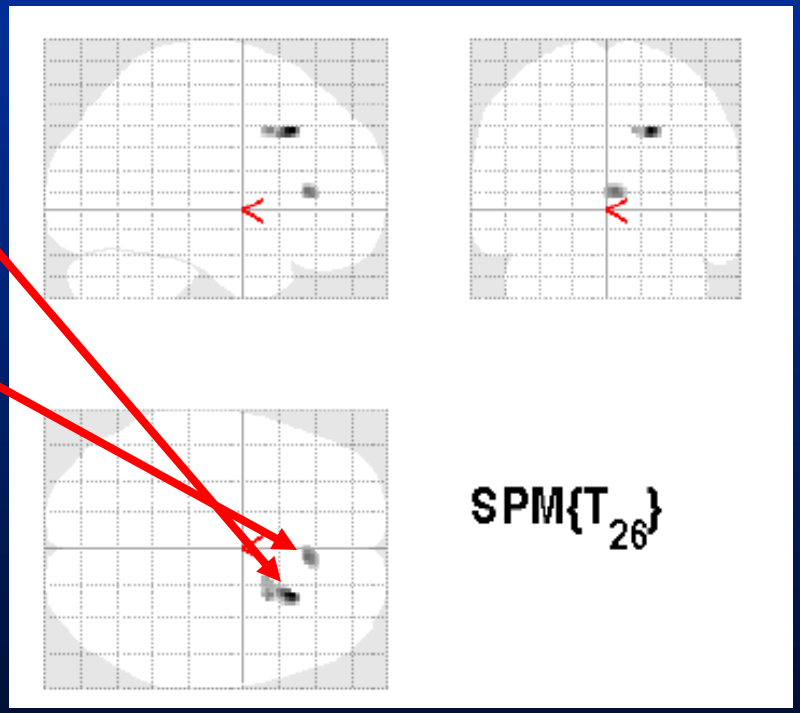
- Middle frontal gyrus (Brodman area 10)
- Insular cortex (Brodman area 13, left and right)
- Caudate body



Results (III)

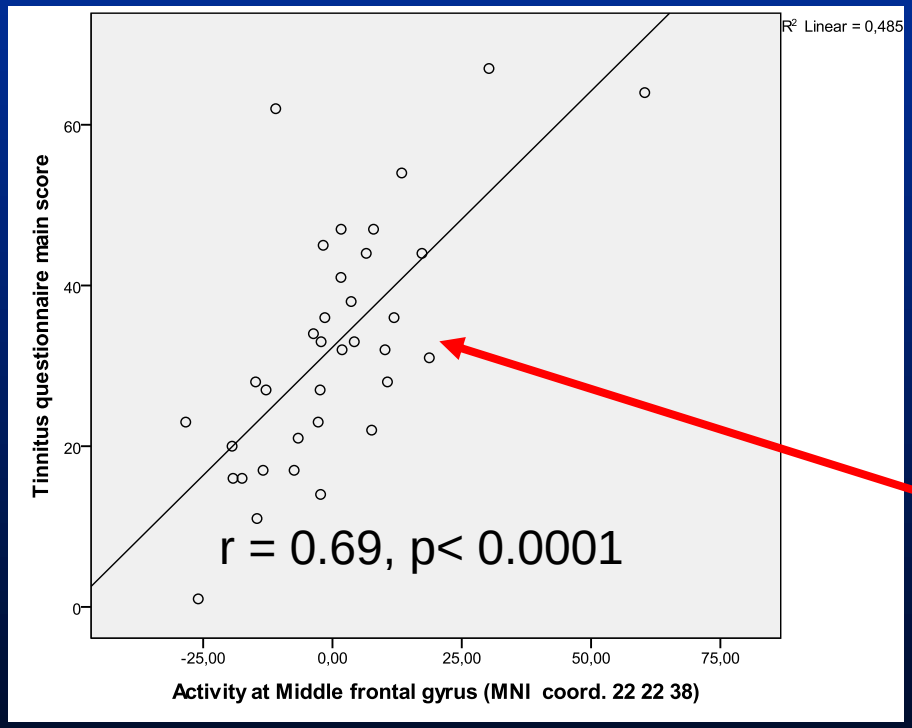
Contrast Tinnitus Tone Stimulation versus Reference Tone (Tinnitus-Subjects)

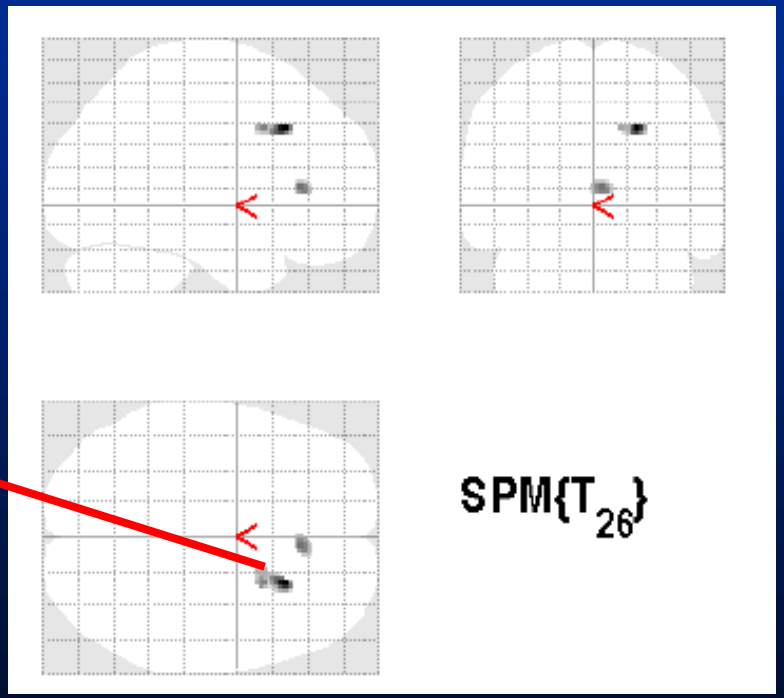
- Middle frontal gyrus (Brodman area 8)
- Anterior cingulate cortex (Brodman area 24)



Results (IV)

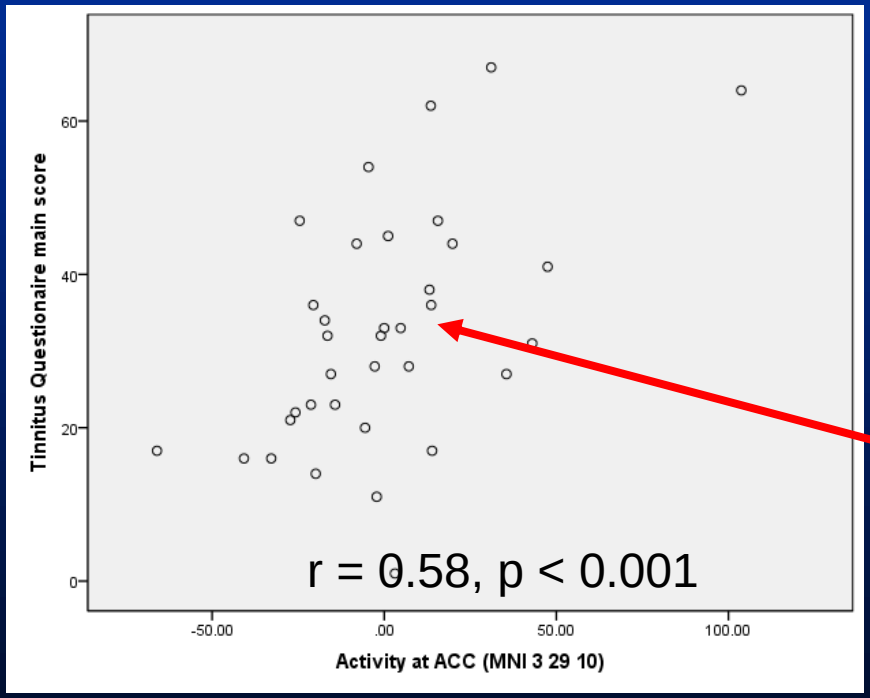
Contrast Tinnitus Tone Stimulation versus SHIFTED Tone (Tinnitus-Subjects)

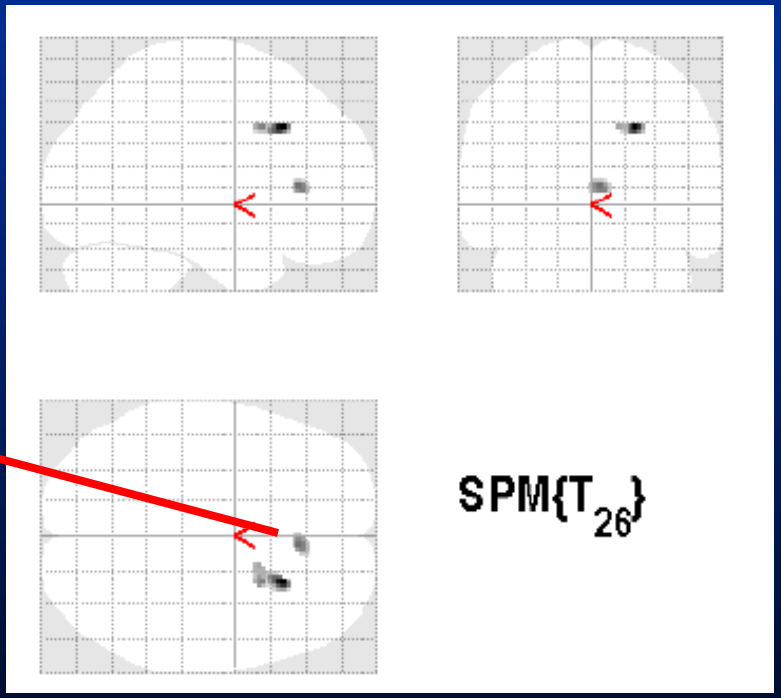




Results (V)

Contrast Tinnitus Tone Stimulation versus SHIFTED Tone (Tinnitus-Subjects)





Results (VI)

Correlations of Activities in MFG (BA 8) and ACC (BA 24) with Tinnitus Questionaire Main Score

		Activity at ACC (BA 24)	Activity at MFG (BA 8)
Activity at ACC (BA 24)	Corr.- Coeff. (Pearson)	1	.588
	Level of Significance		.000
	N	35	35
Activity at MFG (BA 8)	Corr.- Coeff. (Pearson)	.588	1
	Level of Significance	.000	
	N	35	35
Tinnitus Questionaire (Main Score)	Corr.- Coeff. (Pearson)	.531	.696
	Level of Significance	.001	.000
	N	35	35
Beck Depression Inventory (BDI)	Corr.- Coeff. (Pearson)	.587	.403
	Level of Significance	.000	.016
	N	35	35

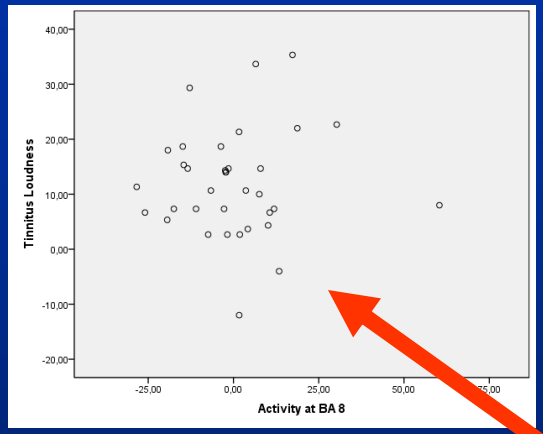
Results (VII)

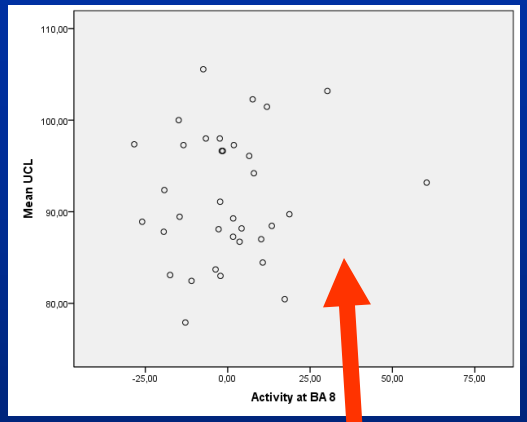
Correlations of Activities in MFG (BA 8) and ACC (BA 24) with Tinnitus Questionaire Main Score

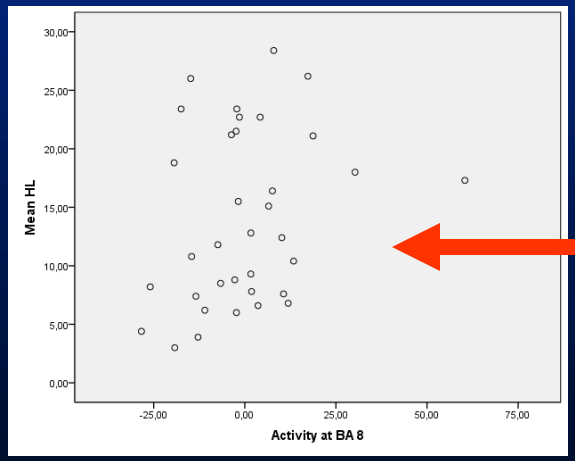
Control variables			Activity at ACC	Activity at BA 8	TQ Main score
BDI	Activity at ACC (MNI 3 29 10)	Correlation	1.000	.474	.336
		Significance	.	.005	.052
	Activity at BA 8 (MNI 22 25 36)	Correlation	.474	1.000	.624
		Significance	.005	.	.000
	TQ main score	Correlation	.336	.624	1.000
		Significance	.052	.000	.

When controlling the correlation of the TQ with the activity at ACC for the BDI score, no significant correlation remains, whereas the correlation TQ and activity at BA 8 is not influenced.

Results (VIII)







No correlation of the activity at ACC (BA 24) or MFG (BA 8) with psychoacoustic data.

Summary and Conclusion (I)

- In tinnitus patients secondary auditory areas (Brodman Area (BA)22 and 42) as well as prefrontal regions (BA 46, 47 and 9) are activated by the reconstructed tinnitus sound.
- Tinnitus patients show a significantly higher activation in prefrontal regions (BA 10), in the insular cortex (BA 13) as well as in the caudate body as compared with non tinnitus patients being stimulated with a tinnitus sound taken from a tinnitus patient.

Summary and Conclusion (II)

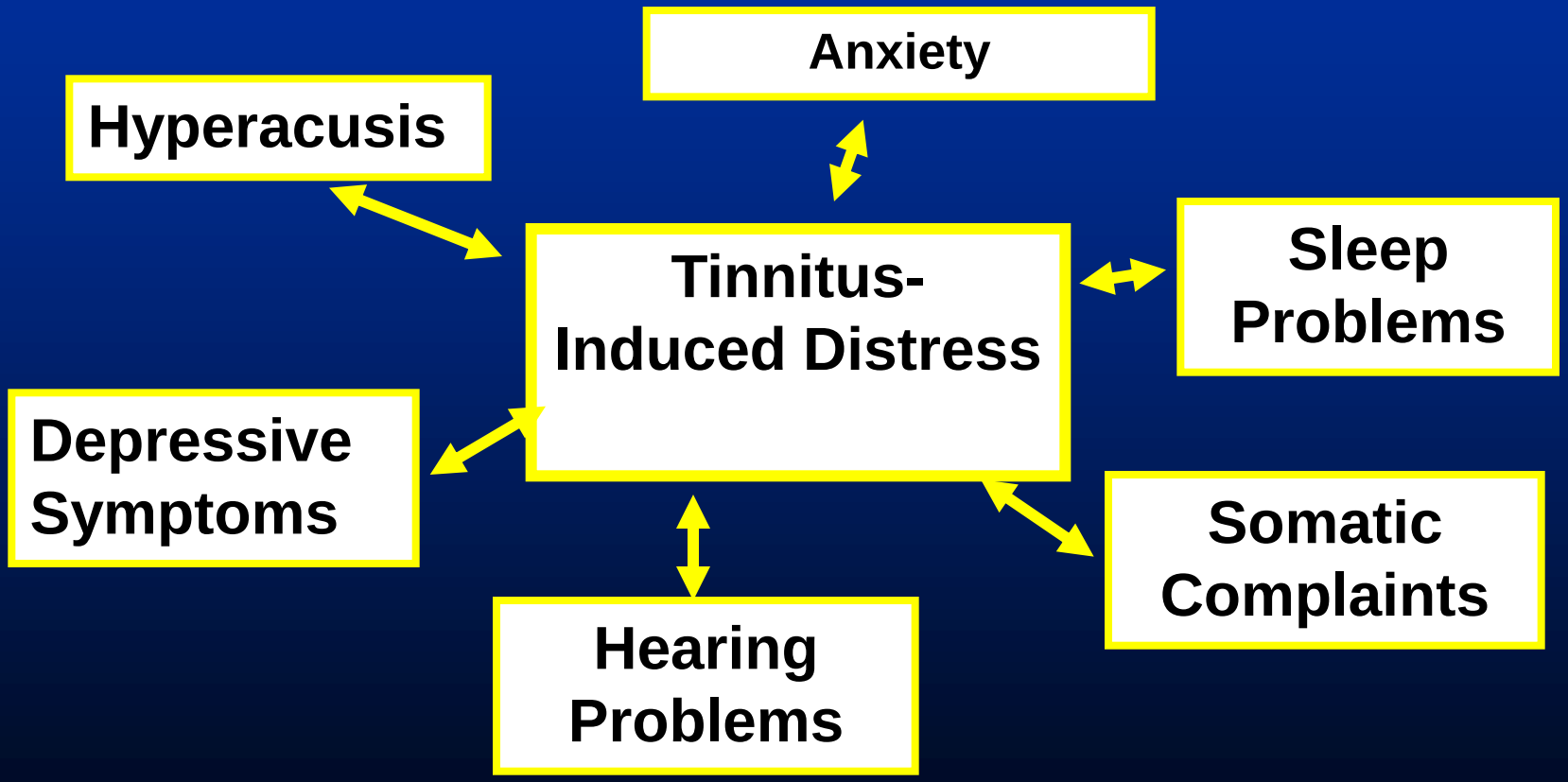
- There is a significantly different activation in response to the reconstructed tinnitus tone as compared to a SHIFTED tone in the right prefrontal cortex (BA 8) and the anterior cingulate cortex (ACC, BA 24).
- Activations in both areas show a significant correlation with tinnitus related distress.

Summary and Conclusion (III)

- **Particularly the prefrontal cortex in BA 8 and the ACC seem to be involved in the development of tinnitus related distress.**

- **The processing in BA 24 (ACC) seems to be influenced by depressive symptoms and anxiety while this is almost not the case in BA 8.**

What are factors contributing to tinnitus- related distress?



Summary and Conclusion (IV)

- The obvious functional differences between areas 8 and 24 in the processing of a reconstructed tinnitus may represent different aspects of tinnitus-related distress relevant for tinnitus treatment.
- Questions for further research:
  - Can this approach be used for the objective evaluation of tinnitus related distress and the subclassificatin of tinnitus patients?
  - Can these findings be replicated with other research methods such as EEG?